IN BRIEF

MULTIPLE SCLEROSIS

Prodromal symptoms might vary between multiple sclerosis subtypes

Patients who develop multiple sclerosis (MS) might exhibit prodromal symptoms that depend on the disease subtype, according to a new paper. Wijnands et al. examined physician encounters during the 5 years before symptom onset in 1,887 patients with relapsing-onset MS (RMS), 171 patients with primary progressive MS (PPMS) and 9,837 matched population controls. The number of physician visits did not differ between the two MS subgroups, or between each subgroup and their controls. However, the types of visit did differ. Patients with RMS or PPMS had increased numbers of neurologist, ophthalmologist and otolaryngologist visits compared with controls. Patients with RMS had more dermatologist visits than either controls or patients with PPMS, and patients with PPMS had more nervous system-related visits than those with RMS.

ORIGINAL ARTICLE Wijnands, J. M. A. et al. The prodrome in relapsing remitting and primary progressive multiple sclerosis. *Eur. J. Neurol.* https://doi.org/10.1111/ene.13925 (2019)

MIGRAINE

Iron deposition in periaqueductal grey matter as a biomarker of chronic migraine

Deposition of iron in the periaqueductal grey matter (PAG) is a potential biomarker for chronic migraine (CM), say researchers. Domínguez and co-workers used 3T MRI to analyse the deposition of iron in the red nucleus, globus pallidus and PAG of 55 patients with CM, 57 patients with episodic migraine (EM) and 25 controls. Patients with CM had increased iron deposition in the red nucleus and PAG compared with patients with EM and controls. Patients with EM had increased iron deposition in the PAG compared with controls. No differences in iron deposition in the globus pallidus were observed between groups. Iron volume in the PAG correlated with serum level of biomarkers of endothelial dysfunction and blood–brain barrier disruption, and a threshold of 240 µl iron in the PAG showed 93% sensitivity and 97% specificity for diagnosis of CM.

ORIGINAL ARTICLE Domínguez, C. et al. Iron deposition in periaqueductal gray matter as a potential biomarker for chronic migraine. *Neurology* https://doi.org/10.1212/WNL.0000000000007047 (2019)

ALZHEIMER DISEASE

Exploring vascular Aβ pathology using microvessel extracts from frozen human brain samples

A new study shows that microvessel extracts can be used to study amyloid-β (Aβ) pathology in the human brain. Bourassa et al. validated a method for generating microvasculature-enriched fractions from frozen samples of human cerebral cortex. They found that $A\beta_{40}$ and $A\beta_{42}$ levels were increased in samples from patients with an AD diagnosis, *APOE*ε4* carriers and individuals with advanced parenchymal cerebral amyloid angiopathy compared with age-matched controls. Vascular concentrations of proteins involved in Aβ clearance were decreased in AD cases and correlated positively with cognitive function and inversely with vascular $A\beta_{40}$ levels. By contrast, levels of a protein needed for Aβ production were increased in AD cases and *APOE*ε4* carriers and correlated negatively with cognitive function and positively with $A\beta_{40}$ levels.

ORIGINAL ARTICLE Bourassa, P. et al. Beta-amyloid pathology in human brain microvessel extracts from the parietal cortex: relation with cerebral amyloid angiopathy and Alzheimer's disease. *Acta Neuropathol.* https://doi.org/10.1007/s00401-019-01967-4 (2019)

PARKINSON DISEASE

Ultrasensitive assay raises hope of plasma PD marker

Through the use of single-molecule array (Simoa) technology, a recent study has shown that plasma levels of α-synuclein are increased in Parkinson disease (PD). The levels of α-synuclein correlated with cognitive impairment, which suggests that this approach could provide a blood-based biomarker of PD.

The use of circulating α-synuclein as a blood-based biomarker of PD has been hindered by low levels of the pathological protein in the plasma. Previous efforts to measure plasma levels with western blotting or enzyme-linked immunosorbent assays have produced conflicting results. Adeline Ng and colleagues attempted to address these difficulties by measuring plasma α-synuclein with Simoa.

"We decided to use Simoa owing to its ultrasensitivity, which has previously been shown to be effective in detecting neurofilament light chain in other neurodegenerative diseases," says Ng. "This study expands the use of ultrasensitive technology in our search for PD biomarkers."

The researchers used Simoa to measure plasma levels of α-synuclein in 170 people with PD and 51 healthy controls. When adjusted for age and sex, overall levels of α-synuclein were significantly higher among patients with PD than among healthy individuals.

Ng and colleagues also assessed the relationship between plasma α-synuclein levels and disease stage, motor performance and cognitive ability. Levels of the protein were not related to disease stage or motor performance, but higher levels were associated with cognitive impairment, indicated by low scores (≤25) on the Mini-Mental State Examination.

PARKINSON DISEASE

Naturally occurring antibodies target Parkinson disease pathology

A new study published in *Acta Neuropathologica* has identified α-synuclein-reactive autoantibodies in the blood of patients with Parkinson disease (PD). In vitro, the antibodies prevented the aggregation of α-synuclein, a protein that accumulates as Lewy bodies and neurites in the brains of people with PD. The findings raise the possibility that these antibodies — and their corresponding epitopes — could serve as early diagnostic biomarkers for PD and might even be harnessed therapeutically.

"Several groups have reported the presence of naturally occurring antibodies to α-synuclein in patients with PD, suggesting that the immune system plays an important role early during the pathogenesis of the disease," comments study leader Gabriel Pascual. "We decided to isolate and characterize such naturally occurring antibodies from patients with PD in an effort to identify disease-relevant epitopes that could be leveraged for therapeutic and biomarker-based approaches."

Pascual and colleagues used BSelex high-throughput, single-cell screening to find memory B cells producing anti-α-synuclein antibodies in blood samples from 25 patients with clinically diagnosed PD. "We previously used the BSelex platform to isolate tau antibodies from immune repertoires of healthy individuals and patients with Alzheimer disease," remarks Pascual.

By expressing antibody genes from the B cells that were identified by BSelex, the researchers isolated ten different anti-α-synuclein antibodies. Three of these antibodies, all of which recognized epitopes in the carboxyl terminus of the α-synuclein molecule, were selected for further study on the